Further Investigations of Hippocampus Chemokine Receptor CXCR3 Expression Level in STZ Induced Hyperglycemic Rat Model

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Background

Hyperglycemia, high blood sugar, is common in preterm infants. The inability of the infant to produce insulin, hypoinsulinism, along with the dextrose given for nutrition are the causes of hyperglycemia. Hyperglycemia in the neonatal period is associated with oxidative stress and potential developmental impairments in preterm infants (*Satrom et al. 2016*).

A previous study model performed by the Rao laboratory showed an upregulation of CXCR3 expression in the hippocampus of postnatal day 6 (P6) rat (*Satrom et al. 2016*). CXCR3 receptor plays a part on T cell recruitment and function (*Groom et al. 2011*). High CXCR3 expression is linked to the inflammatory responses of the hippocampus as a result of hyperglycemia.

The rat pups used in the previous study presented with blood glucose value averaging 200mg/dL. The question is raised on how will CXCR3 expression differ if the pup experiences severe hyperglycemia blood glucose >300mg/dL?

Objective

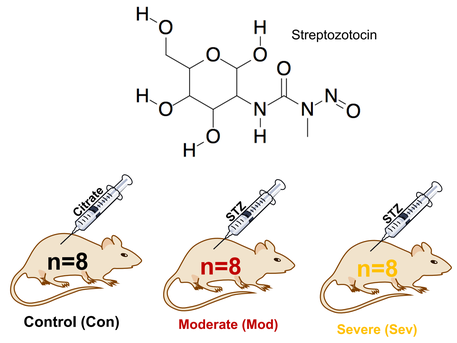
Study the potential difference of CXCR3 mRNA expression level between rat pups who developed moderate hyperglycemia versus rat pups who developed severe hyperglycemia.

Hypothesis

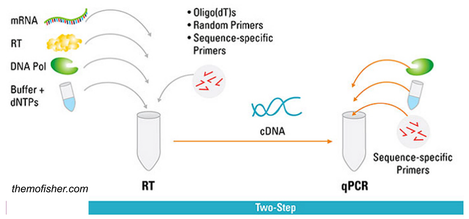
CXCR3 expression level in rat pups with severe hyperglycemia will be significantly higher in comparison with the control and moderate group.

Methods

- Rat pups injected with 100 mg/kg streptozotocin (STZ) IP to induce hyperglycemia (*Graham et al. 2011*) on P1 while the control group received citrate buffer injection.



- Blood glucose and body weight were measured in daily from P2-P6.
- Rat pups killed on P6 and hippocampus was dissected
- RNA extracted
- Two-step RT-qPCR with Rps18 and CXCR3 probes



- One-way ANOVA and T-test were used to test significance of the result of the three groups

Fig 1. Average Body Weight

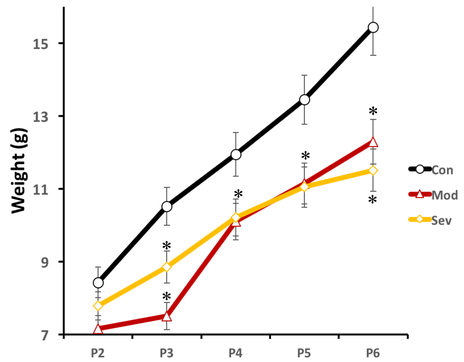


Fig. 2 Average Blood Glucose

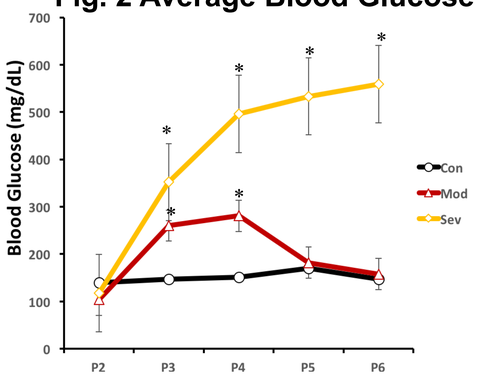
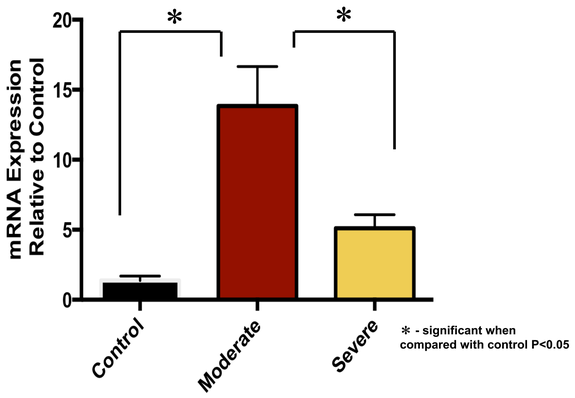


Fig 3. CXCR3 mRNA Expression



Summary

- Rate of weight gain in Mod and Sev groups was noticeably slower compared with the Con group (Fig. 1)
- Blood glucose level of Mod returned to Con level by P6 while Sev glucose level remained higher at P6 (Fig. 2)
- CXCR 3 expression was significant comparing Con vs Mod (P<0.05) (Fig. 3)
- Con vs Sev CXCR3 expression was not significant (P=0.428) (Fig. 3)
- Expression level of CXCR3 between Mod vs Sev was significant (P<0.05) (Fig. 3)

Discussion

The experiment confirmed the result of increased CXCR3 mRNA expression of hippocampus in P6 rat pups with STZ induced hyperglycemia. The expression of CXCR3 level in Sev group was lower than hypothesized. The results may be contributed to a threshold effect. The threshold effect may also be correlated to the expression of CXCL10. CXCL10 binds chemokine to CXCR3 receptor, mRNA expression level could be analyzed for future studies (*Booth et al. 2002*). CXCL10 peaks at 10hr after cell experiences toxicity (*Weering et. al. 2011*). It is possible that Sev tissue was collected after the expression peak of CXCR3 and Mod tissue was collected during the expression peak.

References

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